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Terms	Documents
L35 same (thiol or sulfhydryl or thiolated or SH)	10

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L37

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<u>L37</u>	L35 same (thiol or sulfhydryl or thiolated or SH)	10	<u>L37</u>
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<u>L34</u>	bioadher\$	21	<u>L34</u>
<u>L33</u>	bioadhes\$	937	<u>L33</u>
<u>L32</u>	cysteine near3 (acrylic or pectin or hyaluronic)	5	<u>L32</u>
<u>L31</u>	thiolated near5 (carboxymethylcellulose or alginate or hydroxypropylcellulose)	5	<u>L31</u>
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<u>L29</u>	thiolated adj chitosan	0	<u>L29</u>
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<u>L12</u>	L1 and thio\$	11	<u>L12</u>
<u>L11</u>	L1 and thio\$	11	<u>L11</u>
<u>L10</u>	L1 and thio\$	10	<u>L10</u>
<u>L9</u>	L1 and (thio\$ or sulf\$)	153	<u>L9</u>
<u>L8</u>	L1 and (thio\$ or sulf\$)	148	<u>L8</u>
<u>L7</u>	L1 and (thio\$ or sulf\$)	143	<u>L7</u>
<u>L6</u>	L1 and (thio\$ or sulf\$)	141	<u>L6</u>
<u>L5</u>	L1 and (thio\$ or sulf\$)	133	<u>L5</u>
<u>L4</u>	L1 and (thio\$ or sulf\$)	133	<u>L4</u>
<u>L3</u>	L1 and (thio\$ or sulf\$)	125	<u>L3</u>
<u>L2</u>	L1 and (thio\$ or sulf\$)	33	<u>L2</u>
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NEWS	2	Sep 17	IMSworld Pharmaceutical Company Directory name change to PHARMASEARCH
NEWS	3	Oct 09	Korean abstracts now included in Derwent World Patents Index
NEWS	4	Oct 09	Number of Derwent World Patents Index updates increased
NEWS	5	Oct 15	Calculated properties now in the REGISTRY/ZREGISTRY File
NEWS	6	Oct 22	Over 1 million reactions added to CASREACT
NEWS	7	Oct 22	DGENE GETSIM has been improved
NEWS	8	Oct 29	AAASD no longer available
NEWS	9	Nov 19	New Search Capabilities USPATFULL and USPAT2
NEWS	10	Nov 19	TOXCENTER(SM) - new toxicology file now available on STN
NEWS	11	Nov 29	COPPERLIT now available on STN
NEWS	12	Nov 29	DWPI revisions to NTIS and US Provisional Numbers
NEWS	13	Nov 30	Files VETU and VETB to have open access
NEWS	14	Dec 10	WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
NEWS	15	Dec 10	DGENE BLAST Homology Search
NEWS	16	Dec 17	WELDASEARCH now available on STN
NEWS	17	Dec 17	STANDARDS now available on STN
NEWS	18	Dec 17	New fields for DPCI
NEWS	19	Dec 19	CAS Roles modified
NEWS	20	Dec 19	1907-1946 data and page images added to CA and CAplus
NEWS	21	Jan 25	BLAST(R) searching in REGISTRY available in STN on the Web
NEWS	22	Jan 25	Searching with the P indicator for Preparations
NEWS	23	Jan 29	FSTA has been reloaded and moves to weekly updates
NEWS	24	Feb 01	DKILIT now produced by FIZ Karlsruhe and has a new update frequency
NEWS	25	Feb 19	Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS EXPRESS			February 1 CURRENT WINDOWS VERSION IS V6.0d, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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FILE 'HOME' ENTERED AT 18:56:54 ON 27 FEB 2002

=> file kosmet

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.15	0.15

FULL ESTIMATED COST

FILE 'KOSMET' ENTERED AT 18:57:09 ON 27 FEB 2002

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FILE LAST UPDATED: 22 FEB 2002 <20020222/UP>

FILE COVERS 1968 TO DATE.

=> s mucoadhes?

L1 0 MUCOADHES?

=> s bioadhes?

L2 9 BIOADHES?

=> s thiolated or thiol or sulfhydryl

0 THIOLATED  
43 THIOL  
73 THIOLS  
81 THIOL  
(THIOL OR THIOLS)  
9 SULFHYDRYL  
3 SULFHYDRYLS  
12 SULFHYDRYL  
(SULFHYDRYL OR SULFHYDRYLS)  
L3 87 THIOLATED OR THIOL OR SULFHYDRYL

=> s L2 and L3

L4 0 L2 AND L3

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
1.58	1.73

FULL ESTIMATED COST

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FILE COVERS 1907 - 27 Feb 2002 VOL 136 ISS 9

FILE LAST UPDATED: 26 Feb 2002 (20020226/ED)

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The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the CAS files between 12/27/01 and 1/23/02. As of 1/23/02, the situation has been resolved. Searches and/or SDIs in the H/Z/CA/CAPLUS files incorporating CAS Registry Numbers with the P indicator executed between 12/27/01 and 1/23/02 may be incomplete. See the NEWS message on this topic for more information.

=> s mucoadhes?  
L5 605 MUCOADHES?

=> s bioadhes?  
L6 1486 BIOADHES?

=> s L5 or L6  
L7 1929 L5 OR L6

=> s thiol or sulfhydryl or thiolated  
37769 THIOL  
25109 THIOLS  
51562 THIOL  
(THIOL OR THIOLS)  
20185 SULFHYDRYL  
1527 SULFHYDRYLS  
20802 SULFHYDRYL  
(SULFHYDRYL OR SULFHYDRYLS)  
783 THIOLATED  
L8 69370 THIOL OR SULFHYDRYL OR THIOLATED

=> s L7 and L8  
L9 19 L7 AND L8

=> s L5 and L8  
L10 14 L5 AND L8

=> d L10 1-14 ti

L10 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2002 ACS  
TI Polymer-cysteamine conjugates: new **mucoadhesive** excipients for drug delivery?

L10 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2002 ACS  
TI Multifunctional matrices for oral peptide delivery

L10 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2002 ACS  
TI Development and in vitro evaluation of a **mucoadhesive** vaginal delivery system for progesterone

L10 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2002 ACS  
TI Design and in vitro evaluation of a **mucoadhesive** oral delivery system for a model polypeptide antigen

L10 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2002 ACS  
 TI Synthesis and in vitro evaluation of chitosan-thioglycolic acid conjugates

L10 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2002 ACS  
 TI **Thiolated** polymers - thiomers: development and in vitro evaluation of chitosan-thioglycolic acid conjugates

L10 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2002 ACS  
 TI In vitro evaluation of matrix tablets based on **thiolated** polycarbophil

L10 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2002 ACS  
 TI Improvement in the **mucoadhesive** properties of alginate by the covalent attachment of cysteine

L10 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2002 ACS  
 TI **Mucoadhesive thiolated** polymers: Synthesis and in vitro evaluation of chitosan-thioglycolic acid conjugates

L10 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2002 ACS  
 TI Development of controlled drug release systems based on **thiolated** polymers

L10 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2002 ACS  
 TI Synthesis and characterization of **mucoadhesive thiolated** polymers

L10 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2002 ACS  
 TI Synthesis and in vitro evaluation of chitosan-cysteine conjugates

L10 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2002 ACS  
 TI **Thiolated** polymers: a new generation of **mucoadhesive** polymers

L10 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2002 ACS  
 TI Polymers with **thiol** groups: a new generation of **mucoadhesive** polymers?

=> d L10 1-14 ibib,abs

L10 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2002:115990 CAPLUS  
 TITLE: Polymer-cysteamine conjugates: new **mucoadhesive** excipients for drug delivery?  
 AUTHOR(S): Kast, Constantia E.; Bernkop-Schnurch, Andreas  
 CORPORATE SOURCE: Althanstrasse 14, Institute of Pharmaceutical Technology and Biopharmaceutics, Centre of Pharmacy, University of Vienna, A-1090, Vienna, Austria  
 SOURCE: International Journal of Pharmaceutics (2002), 234(1-2), 91-99  
 CODEN: IJPHDE; ISSN: 0378-5173  
 PUBLISHER: Elsevier Science B.V.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB In the present study, the features of two new **thiolated** polymers-the so-called thiomers-were investigated. Mediated by a carbodiimide cysteamine was covalently attached to sodium CM-cellulose (Na-CMC) and neutralised polycarbophil (Na-PCP). Depending on the

wt.-ratio polymer to cysteamine during the coupling reaction, the resulting CMC-cysteamine conjugate and PCP-cysteamine conjugate showed in max. 43.+-0.15 and 138.+-0.22  $\mu$ mole thiol groups per g polymer (mean+-S.D.; n=3), resp., which were used for further characterization. Tensile studies carried out with the CMC-cysteamine conjugate on freshly excised porcine intestinal mucosa displayed no significant difference ( $P<0.01$ ) improved **mucoadhesion**, whereas, the **mucoadhesive** properties of the PCP-cysteamine conjugate were increased 2.5-fold compared with the unmodified polymer. The swelling behavior of the CMC-cysteamine conjugate was uninfluenced by the covalent attachment of the **sulfhydryl** compd. In contrast the swelling behavior of the PCP-cysteamine conjugate was improved significantly ( $P<0.01$ ) vs. unmodified PCP. Furthermore, in aq. solns. the disintegration time of tablets based on the CMC- and PCP-cysteamine conjugates was prolonged 1.5 and 3.2-fold, resp., in comparison to tablets contg. the corresponding unmodified polymers. According to these results, esp. the PCP-cysteamine conjugate represents a promising new pharmaceutical excipient for various drug delivery systems.

L10 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:934937 CAPLUS  
 TITLE: Multifunctional matrices for oral peptide delivery  
 AUTHOR(S): Bernkop-Schnurch, Andreas; Walker, Greg  
 CORPORATE SOURCE: Institute of Pharmaceutical Technology and  
 Biopharmaceutics, University of Vienna, Vienna,  
 A-1090, Austria  
 SOURCE: Critical Reviews in Therapeutic Drug Carrier Systems  
 (2001), 18(5), 459-501  
 CODEN: CRTSEO; ISSN: 0743-4863  
 PUBLISHER: Begell House, Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The oral administration of peptide drugs represents one of the greatest challenges in pharmaceutical technol. To gain a sufficient bioavailability of these therapeutic agents, various barriers including the mucus-layer barrier, the enzymic barrier, and the membrane barrier have to be overcome. A promising strategy for achieving this goal is the use of multifunctional matrixes. These matrixes are based on polymers that display **mucoadhesive** properties, a permeation-enhancing effect, enzyme-inhibiting properties, and/or a high buffer capacity. Moreover, a sustained or delayed drug release can be provided by delivery systems that contain such polymers. Among them, polyacrylates, cellulose derivs., and chitosan are promising excipients that can also be customized

by chem. modification to improve certain properties. For example, the covalent attachment of **thiol** moieties on these polymers leads to improved **mucoadhesive** and permeation-enhancing properties, and the conjugation of enzyme inhibitors enables the matrixes to provide protection for peptide drugs against enzymic degrdn. The efficacy of multifunctional matrixes in oral peptide delivery has been verified by various in vivo studies that could pave the way for the development of com. viable formulations.

REFERENCE COUNT: 187 THERE ARE 187 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:875467 CAPLUS  
 TITLE: Development and in vitro evaluation of a  
**mucoadhesive** vaginal delivery system for

progesterone  
AUTHOR(S): Valenta, Claudia; Kast, Constantia E.; Harich, Irene;  
Bernkop-Schnurch, Andreas  
CORPORATE SOURCE: University of Vienna, Institute of Pharmaceutical  
Technology and Biopharmaceutics, Vienna, A-1090,  
Austria  
SOURCE: Journal of Controlled Release (2001), 77(3), 323-332  
CODEN: JCREEC; ISSN: 0168-3659  
PUBLISHER: Elsevier Science Ireland Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The purpose of the present study was to design a novel carrier system based on a **mucoadhesive** polymer exhibiting improved properties concerning drug delivery to the vaginal mucosa. This was reached by the covalent attachment of l-cysteine to com. available polyacrylic acid (Carbopol 974P). Mediated by a carbodiimide, increasing amts. of l-cysteine were covalently linked to the polymer. The resulting **thiolated** polyacrylic acid conjugates (NaC974P-Cys) displayed between 24.8 and 45.8 .mu.mol **thiol** groups per g of polymer. Because of the formation of intra- and/or intermol. disulfide bonds, the viscosity of an aq. **thiolated** polymer gel (3%) increased about 50% at pH 7.0 within 1 h. In oscillatory rheol. measurements, it was shown that this increase in viscosity is mainly due to the increase in elasticity. Tensile studies carried out on freshly excised cow vagina demonstrated a significant ( $P < 0.05$ ) increase in the total work of adhesion (TWA) compared to the unmodified polymer. An amt. of 24.8 .mu.mol **thiol** groups per g of polymer resulted in a 1.45-fold increase in the TWA, whereas an amt. of 45.8 .mu.mol showed an even 2.28-fold increase. These improved **mucoadhesive** properties can be explained by the formation of disulfide bonds between the **thiolated** polymer and cysteine rich subdomains of the mucus layer. The release rate of the model drug progesterone from tablets based on microcryst. cellulose serving as the ref. was approx. 1% per h, whereas it was 0.58% per h for the unmodified polymer (NaC974P) and 0.12% per h for the **thiolated** polymer (NaC974P-Cys). Therefore, this **thiolated** polymer is a promising carrier for progesterone providing a prolonged residence time and a controlled drug release.  
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L10 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:723905 CAPLUS  
TITLE: Design and in vitro evaluation of a  
**mucoadhesive** oral delivery system for a model  
polypeptide antigen  
AUTHOR(S): Marschutz, M. K.; Puttipipatkachorn, S.;  
Bernkop-Schnurch, A.  
CORPORATE SOURCE: Institute of Pharmaceutical Technology and  
Biopharmaceutics, Center of Pharmacy, University of  
Vienna, Vienna, 1090, Austria  
SOURCE: Pharmazie (2001), 56(9), 724-729  
CODEN: PHARAT; ISSN: 0031-7144  
PUBLISHER: Govi-Verlag Pharmazeutischer Verlag  
DOCUMENT TYPE: Journal  
LANGUAGE: English



AB A novel **mucoadhesive** drug carrier system has been generated which protects a model polypeptide antigen from degrdn. by the most abundant intestinal proteases. The enzyme inhibitors antipain, chymostatin and elastatinal, resp., were covalently attached to the **mucoadhesive** polymer sodium CM-cellulose (NaCMC) and the inhibitory efficacy of the resulting polymer-inhibitor conjugates was evaluated in vitro. When these inhibitor conjugates were combined with the **thiolated** polymer polycarbophil-cysteine (PCP-Cys), 95.8  $\pm$  3.8% (mean  $\pm$  SD, n = 3) of the incorporated model antigen ovalbumin (OVA) was protected from enzymic degrdn. within 90 min incubation in the presence of an artificial intestinal fluid contg. the pancreatic serine proteases trypsin, chymotrypsin and elastase.

Replacing

the CMC-inhibitor conjugates in the dosage form by unmodified CMC significantly reduced the protective effect to 78.8  $\pm$  4.7% (mean  $\pm$  SD, n = 3), whereas incorporation of the model antigen in a CMC dosage form omitting PCP-Cys protected 72.5  $\pm$  3.2% (mean  $\pm$  SD, n = 3) of OVA from degrdn. within a 90 min incubation period. Further, the incorporation of PCP-Cys resulted in higher cohesiveness within the

dosage

form and controlled drug release of the antigen for a time period of more than 9 h. Results suggest that a delivery system combining **thiolated** polymer and polymer-inhibitor conjugates improves the metabolic stability of the model polypeptide antigen and may therefore be a useful tool for oral protein vaccination.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L10 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:600181 CAPLUS

TITLE: Synthesis and in vitro evaluation of chitosan-thioglycolic acid conjugates

AUTHOR(S): Bernkop-Schnurch, Andreas; Hopf, Thorid E.

CORPORATE SOURCE: Institute of Pharmaceutical Technology and Biopharmaceutics, Center of Pharmacy, University of Vienna, Vienna, A-1090, Austria

SOURCE: Sci. Pharm. (2001), 69(2), 109-118

CODEN: SCPHA4; ISSN: 0036-8709

PUBLISHER: Oesterreichische Apotheker-Verlagsgesellschaft

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The cationic thiomers chitosan-thioglycolic acid (TGA) shows excellent **mucoadhesive** features. In order to deepen the knowledge concerning this new excipient the optimization of its synthesis and a detailed characterization of its properties was the objective of this study. Mediated by increasing quantities of a carbodiimide, thioglycolic acid was covalently attached to chitosan forming amide bonds with the primary amino groups of the polymer. Detd. with Ellman's reagent, 38  $\pm$  3, 104  $\pm$  2, 685  $\pm$  43, and 885  $\pm$  7  $\mu$ mol **thiol** groups (n=3,  $\pm$  SD) were bound per g polymer at carbodiimide concns. of 50,

75,

100, and 125 mM, resp. The immobilized **thiol** groups displayed a comparatively higher reactivity to form disulfide bonds than the **thiol** groups in a corresponding mixt. of chitosan and free unconjugated TGA. In an aq. 0.5% (m/v) chitosan-TGA gel 59  $\pm$  5% of

the

**thiol** groups formed disulfide bonds within 6 h at pH 6.0, whereas merely 5  $\pm$  3% were oxidized in the corresponding phys. mixt. of

chitosan and TGA. Diffusion studies showed that the modified polymer was capable of binding cysteine and cysteine Me ester. The result supports the theory that the improved **mucoadhesive** properties of **thiolated** chitosan are based on the formation of disulfide bonds with cysteine moieties of mucus glycoproteins. Because of its availability via an efficient synthetic pathway and its **mucoadhesive** properties based on the capability to bind cysteine subunits, chitosan-TGA seems to be a promising new excipient for various drug delivery systems.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L10 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:520176 CAPLUS

TITLE: **Thiolated** polymers - thiomers: development and in vitro evaluation of chitosan-thioglycolic acid conjugates

AUTHOR(S): Kast, C. E.; Bernkop-Schnurch, A.

CORPORATE SOURCE: Center of Pharmacy, Institute of Pharmaceutical Technology and Biopharmaceutics, University of Vienna,

Vienna, A-1090, Austria

SOURCE: Biomaterials (2001), 22(17), 2345-2352

CODEN: BIMADU; ISSN: 0142-9612

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The aim of this study was to improve **mucoadhesive** properties of chitosan by the covalent attachment of **thiol** moieties to this cationic polymer. Mediated by a carbodiimide, thioglycolic acid (TGA) was

covalently attached to chitosan. This was achieved by the formation of amide bonds between the primary amino groups of the polymer and the carboxylic acid group of TGA. Dependent on the pH-value and the wt. ratio

of polymer to TGA during the coupling reaction the resulting **thiolated** polymers, the so-called thiomers, displayed 6.58, 9.88, 27.44, and 38.23  $\mu\text{mole thiol groups per g polymer}$ . Tensile studies carried out with these chitosan-TGA conjugates on freshly excised porcine intestinal mucosa demonstrated a 6.3-, 8.6-, 8.9-, and 10.3-fold increase in the total work of adhesion (TWA) compared to the unmodified polymer, resp. In contrast, the combination of chitosan and free unconjugated TGA showed almost no **mucoadhesion**. These data were in good correlation with further results obtained by another **mucoadhesion** test demonstrating a prolonged residence time of **thiolated** chitosan on porcine mucosa. The swelling behavior of all conjugates was thereby exactly in the same range as for an unmodified polymer pretreated in the same way. Furthermore, it could be shown that chitosan-TGA conjugates are still biodegradable by the glycosidase lysozyme. According to these results, chitosan-TGA conjugates represent

a promising tool for the development of **mucoadhesive** drug delivery systems.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L10 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:350505 CAPLUS  
DOCUMENT NUMBER: 136:107353  
TITLE: In vitro evaluation of matrix tablets based on  
**thiolated** polycarbophil  
AUTHOR(S): Clausen, Andreas E.; Bernkop-Schnurch, Andreas  
CORPORATE SOURCE: Center of Pharmacy, Institute of Pharmaceutical  
Technology and Biopharmaceutics, University of  
Vienna,  
Vienna, Austria  
SOURCE: Pharmazeutische Industrie (2001), 63(3), 312-317  
CODEN: PHINAN; ISSN: 0031-711X  
PUBLISHER: Editio Cantor Verlag  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Based on **thiolated** polycarbophil, a **mucoadhesive**  
peptide drug delivery system with improved stability and release  
properties has been established. Mediated by a carbodiimide, L-cysteine  
was covalently linked to polycarbophil (PCP). The amt. of cysteine  
moieties on the polymer was in the range of 72.6.+-.5.8 .mu.mol/g  
polymer.

Disintegration studies with tablets of **thiolated** PCP (PCP-Cys)  
demonstrated a stability for 48.3.+-.1.5 min at 37.degree. in 100 mM  
Tris-HCl pH 6.8, whereas tablets of the corresponding unmodified polymer  
(PCP) disintegrated within a time period of 13.8.+-.1.6 min (mean .+-.  
SD,

n = 3). During these disintegration studies the amt. of **thiol**  
groups decreased in tablets consisting exclusively of PCP-Cys by  
80.0.+-.4.5%, suggesting that the formation of inter- and/or intramol.  
disulfide bonds is responsible for this strongly improved stability of  
tablets based on the **thiolated** polymer. Further expts.  
demonstrated that this decrease in **thiol** groups can be lowered  
to 64.2.+-.0.8% by substituting 60 % of the **thiolated** polymer by  
mannitol. Release studies of the fluorescence labeled model drug insulin  
showed that an almost zero-order release kinetic can be provided by the  
use of **thiolated** polycarbophil as carrier matrix. The results  
represent helpful information in order to improve the stability and  
release properties of matrix tablets based on **mucoadhesive**  
polymers.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR  
THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L10 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:237207 CAPLUS  
DOCUMENT NUMBER: 135:157488  
TITLE: Improvement in the **mucoadhesive** properties  
of alginate by the covalent attachment of cysteine  
AUTHOR(S): Bernkop-Schnurch, A.; Kast, C. E.; Richter, M. F.  
CORPORATE SOURCE: Center of Pharmacy, Institute of Pharmaceutical  
Technology and Biopharmaceutics, University of  
Vienna,  
Vienna, A-1090, Austria  
SOURCE: J. Controlled Release (2001), 71(3), 277-285  
CODEN: JCREEC; ISSN: 0168-3659  
PUBLISHER: Elsevier Science Ireland Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The purpose of the present study was to improve the **mucoadhesive**

properties of alginate by the covalent attachment of cysteine. Mediated by a carbodiimide, L-cysteine was covalently linked to the polymer. The resulting **thiolated** alginate displayed  $340.4 \pm 74.9 \text{ } \mu\text{mol}$  **thiol** groups per g conjugate (means  $\pm$  S.D.; n=4). Within 2 h the viscosity of an aq. mucus/alginate-cysteine conjugate mixt. pH 7.0 increased at 37.degree.C by more than 50% compared to a mucus/alginate mixt., indicating enlarged interactions between the mucus and the **thiolated** polymer. Tensile studies carried out on freshly excised porcine intestinal mucosa demonstrated a total work of adhesion (TWA) of  $25.8 \pm 0.6$  and  $101.6 \pm 36.1 \text{ } \mu\text{J}$  for alginate and the

alginate-cysteine

conjugate, resp. (means  $\pm$  S.D.; n=5). The max. detachment force (MDF) was thereby in good correlation with the TWA. Due to the immobilization of cysteine, the swelling velocity of the polymer was significantly accelerated ( $P < 0.05$ ). In aq. media the alginate-cysteine conjugate was capable of forming inter- and/or intramol. disulfide bonds. Because of this crosslinking process within the polymeric network, the cohesive properties of the conjugate were also improved. Tablets comprising the unmodified polymer disintegrated within  $49 \pm 14.5$  min, whereas tablets

of

**thiolated** alginate remained stable for  $148.8 \pm 39.1$  min (means  $\pm$  S.D.; n=3). These features should render **thiolated** alginate useful as excipient for various drug delivery systems providing an improved stability and a prolonged residence time on certain mucosal epithelia.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L10 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:672530 CAPLUS

DOCUMENT NUMBER: 134:136581

TITLE: **Mucoadhesive thiolated polymers:**

Synthesis and in vitro evaluation of chitosan-thioglycolic acid conjugates

AUTHOR(S): Kast, C. E.; Freudl, J.; Bernkop-Schnurch, A.  
CORPORATE SOURCE: Center of Pharmacy, Institute of Pharmaceutical Technology and Biopharmaceutics, University of

Vienna,

Vienna, A-1090, Austria

SOURCE: Proc. Int. Symp. Controlled Release Bioact. Mater. (2000), 27th, 1222-1223

CODEN: PCRMEY; ISSN: 1022-0178

PUBLISHER: Controlled Release Society, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The covalent attachment of thioglycolic acid to cationic chitosan leads to

polymers exhibiting strongly improved **mucoadhesive** properties.

Due to the formation of inter- and/or intrachain disulfide bonds based on an oxidn. process, the cohesive properties of the polymer could be improved as well.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L10 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:152364 CAPLUS

DOCUMENT NUMBER: 133:94406

TITLE: Development of controlled drug release systems based on **thiolated** polymers  
AUTHOR(S): Bernkop-Schnurch, A.; Scholler, S.; Biebel, R. G.  
CORPORATE SOURCE: Center of Pharmacy, Institute of Pharmaceutical Technology, University of Vienna, Vienna, A-1090, Austria  
SOURCE: J. Controlled Release (2000), 66(1), 39-48  
CODEN: JCREEC; ISSN: 0168-3659  
PUBLISHER: Elsevier Science Ireland Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The purpose of the present study was to generate **mucoadhesive** matrix-tablets based on **thiolated** polymers. Mediated by a carbodiimide, L-cysteine was thereby covalently linked to polycarbophil (PCP) and sodium CM-cellulose (CMC). The resulting **thiolated** polymers displayed 100 and 12804  $\mu\text{mol thiol groups/g}$ , resp. In aq. solns. these modified polymers were capable of forming inter- and/or intramol. disulfide bonds. The rate of this process augmented with increase of the polymer- and decrease of the proton-concn. The oxidn. proceeded more rapidly within **thiolated** PCP than within **thiolated** CMC. Due to the formation of disulfide bonds within **thiol**-contg. polymers, the stability of matrix-tablets based on such polymers could be strongly improved. Whereas tablets based on the corresponding unmodified polymer disintegrated within 2 h, the swollen carrier matrix of **thiolated** CMC and PCP remained stable for 6.2 h and more than 48 h, resp. Release studies of the model drug rifampicin demonstrated that a controlled release can be provided by **thiolated** polymer tablets. The combination of high stability, controlled drug release and **mucoadhesive** properties renders matrix-tablets based on **thiolated** polymers useful as novel drug delivery systems.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L10 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:123953 CAPLUS

DOCUMENT NUMBER: 132:298657

TITLE: Synthesis and characterization of **mucoadhesive thiolated** polymers

AUTHOR(S): Bernkop-Schnurch, A.; Steininger, S.

CORPORATE SOURCE: Center of Pharmacy, Institute of Pharmaceutical Technology, University of Vienna, Vienna, A-1090, Austria

SOURCE: Int. J. Pharm. (2000), 194(2), 239-247

CODEN: IJPHDE; ISSN: 0378-5173

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB This study examd. various factors influencing the **mucoadhesive** properties of **thiolated** polymers (thiomers), which are capable of forming covalent bonds with **thiol** sub-structures of the mucus glycoprotein. Mediated by a carbodiimide, L-cysteine was therefore covalently bound to polycarbophil (PCP) and to CM-cellulose (CMC). The resulting polymer conjugates displayed 12.3 and 22.3  $\mu\text{mol thiol groups per g}$ , resp. Whereas the swelling behavior of tablets based on CMC

was not markedly influenced by the immobilization of cysteine, it was

improved significantly ( $P < 0.05$ ) in case of PCP. Tensile studies carried out with the unmodified and **thiolated** polymers of pH 3, 5 and 7, resp., revealed that only if the polymer displays a pH-value of 5, the total work of adhesion can be improved significantly due to the covalent attachment of **thiol** groups. These results were in good agreement with a new **mucoadhesion** test system described here taking also the cohesiveness of the delivery system into account. The results represent helpful basic information in order to improve the **mucoadhesive** properties of **thiolated** polymers.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L10 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:31626 CAPLUS

DOCUMENT NUMBER: 132:98016

TITLE: Synthesis and in vitro evaluation of  
chitosan-cysteine

conjugates

AUTHOR(S): Bernkop-Schnurch, Andreas; Brandt, Ursula-Maria;  
Clausen, Andreas E.

CORPORATE SOURCE: Institut Pharmazeutische Technologie,  
Pharmazie-Zentrum, Univ. Wien, Vienna, A-1090,

Austria

SOURCE: Sci. Pharm. (1999), 67(4), 197-208

CODEN: SCPHA4; ISSN: 0036-8709

PUBLISHER: Oesterreichische Apotheker-Verlagsgesellschaft

DOCUMENT TYPE: Journal

LANGUAGE: German

AB Mediated by a water-sol. carbodiimide cysteine was covalently attached to chitosan. According to the amt. of carbodiimide during the coupling reaction, 0.25, 0.7, and 1.2% of Cys were thereby bound to the polymer. Whereas the **mucoadhesive** properties of chitosan could not be improved due to this modification, the stability of matrix tablets based on **thiolated** chitosan might be strongly improved because of the formation of inter- and/or intramol. disulfide bonds within these polymers. This oxidative process can be accelerated at higher temps. and by lowering the proton concn. on the polymer. Permeation studies carried out by chambers with freshly excised intestinal mucosa from guinea pigs demonstrated furthermore an improved permeation enhancing effect of chitosan due to the covalent attachment of Cys on it.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L10 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:758076 CAPLUS

DOCUMENT NUMBER: 132:298491

TITLE: **Thiolated** polymers: a new generation of  
**mucoadhesive** polymers

AUTHOR(S): Bernkop-Schnuerch, A.

CORPORATE SOURCE: Cent. of Pharm., Inst. of Pharm. Technol., Univ. of  
Vienna, Vienna, A-1090, Austria

SOURCE: Farm. Vestn. (Ljubljana) (1999), 50(Pos. Stev.),  
268-269

CODEN: FMVTAV; ISSN: 0014-8229

PUBLISHER: Slovensko Farmacevtsko Drustvo

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 4 refs. of the **mucoadhesion**, cohesiveness, and penetration-enhancing capabilities of thiomers (**thiolated** polymers) and their action in inhibiting Zn proteinases. These polymers include conjugates of cysteine with polycarbophil, chitosan, and Na CM-cellulose, and are believed to interact with cysteine-rich subdomains of mucus glycoproteins.

L10 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:408906 CAPLUS

DOCUMENT NUMBER: 131:174949

TITLE: Polymers with **thiol** groups: a new generation of **mucoadhesive** polymers?

AUTHOR(S): Bernkop-Schnurch, Andreas; Schwarz, Veronika; Steininger, Sonja

CORPORATE SOURCE: Center of Pharmacy, Institute of Pharmaceutical Technology, University of Vienna, Vienna, A-1090, Austria

SOURCE: Pharm. Res. (1999), 16(6), 876-881

CODEN: PHREEB; ISSN: 0724-8741

PUBLISHER: Kluwer Academic/Plenum Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The **mucoadhesive** properties of polycarbophil were improved by the introduction of **sulphydryl** groups. Mediated by a carbodiimide, cysteine was covalently bound to polycarbophil (PCP) forming

amide bonds between the primary amino group of the amino acid and the carboxylic acid moieties of the polymer. The amt. of covalently attached cysteine and the formation of disulfide bonds within the modified polymer were detd. by quantifying the share of **thiol** groups on the polymer conjugates with Ellman's reagent. The adhesive properties of polycarbophil-cysteine conjugates were evaluated in vitro on excised porcine intestinal mucosa by detg. the total work of adhesion (TWA). Depending on the wt.-ratio of polycarbophil to cysteine at the coupling reaction, e.g., 16:1 and 2:1, 0.6  $\pm$  0.7  $\mu$ mole and 5.3  $\pm$  2.4  $\mu$ mole cysteine, resp., were covalently bound per g polymer. The modified polymer displayed improved internal cohesive properties due to the formation of interchain disulfide bonds within the polymer in aq. solns. at pH-values above 5. Adhesion studies revealed strongly improved adhesive properties. Whereas the TWA was detd. to be 104  $\pm$  21  $\mu$ J for the unmodified polymer, it was 191  $\pm$  47  $\mu$ J for the polymer-cysteine conjugate 16:1 and 280  $\pm$  67  $\mu$ J for the polymer-cysteine conjugate 2:1. Polymers with **thiol** groups might represent a new generation of **mucoadhesive** polymers displaying comparatively stronger adhesive properties.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS

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=> s mucoadhes?

L11 365 MUCOADHES?

=> s bioadhes?

L12 623 BIOADHES?

=> s L11 or L12

L13 908 L11 OR L12

=> s thiol or sulfhydryl or thiolated

16699 THIOL

5156 THIOLS

19661 THIOL

(THIOL OR THIOLS)

14530 SULFHYDRYL

908 SULFHYDRYLS

15050 SULFHYDRYL

(SULFHYDRYL OR SULFHYDRYLS)

262 THIOLATED

L14 33274 THIOL OR SULFHYDRYL OR THIOLATED

=> s L13 and L14

L15 5 L13 AND L14

=> d L15 1-5 ti

L15 ANSWER 1 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

TI Development and in vitro evaluation of a **mucoadhesive** vaginal  
delivery system for progesterone.

L15 ANSWER 2 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

TI Improvement in the **mucoadhesive** properties of alginate by the  
covalent attachment of cysteine.

L15 ANSWER 3 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

TI Development of controlled drug release systems based on **thiolated**  
polymers.

L15 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

TI Synthesis and characterisation of **mucoadhesive thiolated**  
polymers.

L15 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

TI Polymers with **thiol** groups: A new generation of  
**mucoadhesive** polymers.

=> d L15 1-5 ibib



L15 ANSWER 1 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
ACCESSION NUMBER: 2002:161356 BIOSIS  
DOCUMENT NUMBER: PREV200200161356  
TITLE: Development and in vitro evaluation of a  
**mucoadhesive** vaginal delivery system for  
progesterone.  
AUTHOR(S): Valenta, Claudia (1); Kast, Constantia E.; Harich, Irene;  
Bernkop-Schnurch, Andreas  
CORPORATE SOURCE: (1) Institute of Pharmaceutical Technology and  
Biopharmaceutics, University of Vienna, Althanstrasse 14,  
A-1090, Vienna: claudia.valenta@univie.ac.at Austria  
SOURCE: Journal of Controlled Release, (13 December, 2001) Vol.  
77,  
No. 3, pp. 323-332.  
<http://www.elsevier.com/locate/jconrel>.  
print.  
ISSN: 0168-3659.  
DOCUMENT TYPE: Article  
LANGUAGE: English

L15 ANSWER 2 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
ACCESSION NUMBER: 2001:273548 BIOSIS  
DOCUMENT NUMBER: PREV200100273548  
TITLE: Improvement in the **mucoadhesive** properties of  
alginate by the covalent attachment of cysteine.  
AUTHOR(S): Bernkop-Schnuerch, Andreas (1); Kast, Constantia E.;  
Richter, Martina F.  
CORPORATE SOURCE: (1) Center of Pharmacy, Institute of Pharmaceutical  
Technology and Biopharmaceutics, University of Vienna,  
Althanstr. 14, A-1090, Vienna: andreas.bernkop-  
schnuerch@univie.ac.at Austria  
SOURCE: Journal of Controlled Release, (28 April, 2001) Vol. 71,  
No. 3, pp. 277-285. print.  
ISSN: 0168-3659.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
SUMMARY LANGUAGE: English

L15 ANSWER 3 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
ACCESSION NUMBER: 2000:235356 BIOSIS  
DOCUMENT NUMBER: PREV200000235356  
TITLE: Development of controlled drug release systems based on  
**thiolated** polymers.  
AUTHOR(S): Bernkop-Schnuerch, Andreas (1); Scholler, Sabine; Biebel,  
Regina G.  
CORPORATE SOURCE: (1) Center of Pharmacy, Institute of Pharmaceutical  
Technology, University of Vienna, Althanstr. 14, A-1090,  
Vienna Austria  
SOURCE: Journal of Controlled Release, (May 3, 2000) Vol. 66, No.  
1, pp. 39-48.  
ISSN: 0168-3659.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
SUMMARY LANGUAGE: English

L15 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
ACCESSION NUMBER: 2000:119913 BIOSIS  
DOCUMENT NUMBER: PREV200000119913  
TITLE: Synthesis and characterisation of **mucoadhesive**  
**thiolated** polymers.

AUTHOR(S): Bernkop-Schnuerch, A. (1); Steininger, S.  
 CORPORATE SOURCE: (1) Center of Pharmacy, Institute of Pharmaceutical  
 Technology, University of Vienna, Althanstrasse 14,  
 A-1090,  
 Vienna Austria  
 SOURCE: International Journal of Pharmaceutics (Amsterdam), (Jan.  
 25, 2000) Vol. 194, No. 2, pp. 239-247.  
 ISSN: 0378-5173.  
 DOCUMENT TYPE: Article  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English

L15 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
 ACCESSION NUMBER: 1999:319303 BIOSIS  
 DOCUMENT NUMBER: PREV199900319303  
 TITLE: Polymers with **thiol** groups: A new generation of  
**mucoadhesive** polymers.  
 AUTHOR(S): Bernkop-Schnurch, Andreas (1); Schwarz, Veronika;  
 Steininger, Sonja  
 CORPORATE SOURCE: (1) Center of Pharmacy, Institute of Pharmaceutical  
 Technology, University of Vienna, Althanstr. 14, Vienna,  
 A-1090 Austria  
 SOURCE: Pharmaceutical Research (New York), (June, 1999) Vol. 16,  
 No. 6, pp. 876-881.  
 ISSN: 0724-8741.  
 DOCUMENT TYPE: Article  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English

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FULL ESTIMATED COST	12.67	64.26
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FILE 'KOSMET' ENTERED AT 18:57:09 ON 27 FEB 2002

L1	0 S MUCOADHES?
L2	9 S BIOADHES?
L3	87 S THIOLATED OR THIOL OR SULFHYDRYL
L4	0 S L2 AND L3

FILE 'CAPLUS' ENTERED AT 18:58:13 ON 27 FEB 2002

L5	605 S MUCOADHES?
L6	1486 S BIOADHES?

L7            1929 S L5 OR L6  
L8            69370 S THIOL OR SULFHYDRYL OR THIOLATED  
L9            19 S L7 AND L8  
L10           14 S L5 AND L8

FILE 'BIOSIS' ENTERED AT 19:08:31 ON 27 FEB 2002

L11           365 S MUCOADHES?  
L12           623 S BIOADHES?  
L13           908 S L11 OR L12  
L14           33274 S THIOL OR SULFHYDRYL OR THIOLATED  
L15           5 S L13 AND L14

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